

Patent  
674537-2001**AMENDMENT**

Please amend the application without prejudice, without admission, without surrender of subject matter and without intention of creating any estoppel as to equivalents, as follows.

**In the Claims**

1-64. (Cancelled)

65. (Currently amended) A complex formed between (i) an antibody or biologically active fragment thereof ~~derived~~ from a first species and (ii) a bifunctional molecule, the bifunctional molecule comprising a binding region of non-antibody origin which binds to the antibody of the first species or to one or more non-naturally occurring groups provided thereon, and a constant region ~~derived~~ from an antibody of a second species, the constant region comprising at least one C<sub>H</sub> domain or an epitope thereof, wherein the binding region and the constant region are linked directly or are separated by a linker molecule of between 1 and 20 amino acids in length, and wherein the bifunctional molecule is bound to a location on the antibody of the first species or to one or more non-naturally occurring groups provided thereon, which does not hinder binding between the antibody and its specific antigen.

66. (Currently amended) A complex formed between (i) an antibody or biologically active fragment thereof ~~derived~~ from a first species and (ii) a bifunctional molecule, the bifunctional molecule comprising a binding region of non-antibody origin which binds to the antibody of the first species or to one or more non-naturally occurring groups provided thereon, and a constant region ~~derived~~ from an antibody of a second species, the constant region comprising at least one C<sub>H</sub> domain or an epitope thereof, wherein the binding region has a K<sub>D</sub> for the antibody of the first species, or a group provided thereon, of less than 10<sup>-6</sup> M, and wherein the bifunctional molecule is bound to a location on the antibody of the first species or to one or more non-naturally occurring groups provided thereon, which does not hinder binding between the antibody and its specific antigen.

67. (Original) A complex according to claim 66 in which the binding region has a K<sub>D</sub> for the antibody of the first species, or a group provided thereon, of less than 10<sup>-8</sup> M.

68. (Currently amended) A complex according to claim 65 in which the bifunctional molecule binds directly to the antibody ~~derived~~ from the first species.

69. (Currently amended) A complex according to claim 68 in which the binding region is ~~derived from~~ a protein selected from the group consisting of, *Streptococcal* protein G,

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Staphylococcal aureus protein A, and Peptostreptococcus magnus protein L, or a fragment thereof.

70. (Original) A complex according to claim 69 in which the binding region comprises fragment B of *Staphylococcus aureus* protein A.

71. (Original) A complex according to claim 68 in which the binding region comprises a mouse Fc  $\gamma$  receptor or fragment thereof.

72. (Currently amended) A complex according to claim 68 in which the binding region comprises [[a]] histidine rich glycoprotein.

73. (Currently amended) A complex formed between (i) an antibody or biologically active fragment thereof derived from a first species and (ii) a bifunctional molecule, the bifunctional molecule comprising a binding region of non-antibody origin which binds to the antibody of the first species or to one or more non-naturally occurring groups provided thereon, and a constant region derived from an antibody of a second species, the constant region comprising at least one C<sub>H</sub> domain or an epitope thereof, wherein the binding region binds to one or more groups provided on the antibody of the first species, in a location which does not hinder binding between the antibody and its specific antigen.

74. (Original) A complex according to claim 73 in which the group(s) is a biotin molecule and the binding region comprises streptavidin or a fragment thereof.

75. (Currently amended) A complex formed between (i) an antibody or biologically active fragment thereof derived from a first species and (ii) a bifunctional molecule, the bifunctional molecule comprising a binding region of non-antibody origin which binds to the antibody of the first species or to one or more non-naturally occurring groups provided thereon, and a constant region derived from an antibody of a second species, the constant region comprising at least one C<sub>H</sub> domain or an epitope thereof, wherein the constant region comprises one or more constant domains derived from an IgM antibody, and wherein the bifunctional molecule is bound to a location on the antibody of the first species or to one or more non-naturally occurring groups provided thereon, which does not hinder binding between the antibody and its specific antigen.

76. (Original) A complex according to claim 75 in which the constant region comprises one or more C<sub>H</sub>3 $\mu$  domains.

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77. (Currently amended) A complex formed between (i) an antibody or biologically active fragment thereof ~~derived~~ from a first species and (ii) a bifunctional molecule, the bifunctional molecule comprising a binding region of non-antibody origin which binds to the antibody of the first species or to one or more non-naturally occurring groups provided thereon, and a constant region ~~derived~~ from an antibody of a second species, the constant region comprising at least one C<sub>H</sub> domain or an epitope thereof, wherein the constant region comprises one or more constant domains ~~derived~~ from an IgG antibody, and wherein the bifunctional molecule is bound to a location on the antibody of the first species or to one or more non-naturally occurring groups provided thereon, which does not hinder binding between the antibody and its specific antigen.

78. (Original) A complex according to claim 77 in which the constant region comprises one or more C<sub>H</sub>3γ domains.

79. (Currently amended) A complex formed between (i) an antibody or biologically active fragment thereof ~~derived~~ from a first species and (ii) a bifunctional molecule, the bifunctional molecule comprising a binding region of non-antibody origin which binds to the antibody of the first species or to one or more non-naturally occurring groups provided thereon, and a constant region ~~derived~~ from an antibody of a second species, the constant region comprising at least one C<sub>H</sub> domain or an epitope thereof, wherein the constant region comprises one or more constant domains ~~derived~~ from an IgA antibody, and wherein the bifunctional molecule is bound to a location on the antibody of the first species or to one or more non-naturally occurring groups provided thereon, which does not hinder binding between the antibody and its specific antigen.

80. (Currently amended) A complex formed between (i) an antibody or biologically active fragment thereof ~~derived~~ from a first species and (ii) a bifunctional molecule, the bifunctional molecule comprising a binding region of non-antibody origin which binds to the antibody of the first species or to one or more non-naturally occurring groups provided thereon, and a constant region ~~derived~~ from an antibody of a second species, the constant region comprising at least one C<sub>H</sub> domain or an epitope thereof, wherein the antibody constant region comprises or consists of a non-naturally occurring combination of immunoglobulin C<sub>H</sub> domains or epitopes thereof, and wherein the bifunctional molecule is bound to a location on the antibody

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of the first species or to one or more non-naturally occurring groups provided thereon, which does not hinder binding between the antibody and its specific antigen.

81. (Original) A complex according to claim 65 in which the antibody constant region comprises or consists of a single C<sub>H</sub> domain.

82. (Original) A complex according to claim 65 in which the first species is a rat or mouse.

83. (Currently amended) A complex formed between (i) an antibody or biologically active fragment thereof ~~derived~~ from a first species and (ii) a bifunctional molecule, the bifunctional molecule comprising a binding region of non-antibody origin which binds to the antibody of the first species or to one or more non-naturally occurring groups provided thereon, and a constant region ~~derived~~ from an antibody of a second species, the constant region comprising at least one C<sub>H</sub> domain or an epitope thereof, wherein the second species is a human, and wherein the bifunctional molecule is bound to a location on the antibody of the first species or to one or more non-naturally occurring groups provided thereon, which does not hinder binding between the antibody and its specific antigen.

84-89. (Cancelled)

90. (Currently amended) A complex formed between (i) an antibody or biologically active fragment thereof ~~derived~~ from a first species and (ii) a bifunctional molecule, the bifunctional molecule consisting of a binding region of non-antibody origin which binds to the antibody of the first species or to one or more non-naturally occurring groups provided thereon, and a constant region ~~derived~~ from an antibody of a second species, the constant region consisting of at least one C<sub>H</sub> domain or an epitope thereof, wherein the bifunctional molecule is bound to a location on the antibody of the first species or to one or more non-naturally occurring groups provided thereon, which does not hinder binding between the antibody and its specific antigen.

91. (New) A complex formed between (i) an antibody or biologically active fragment thereof from a first species and (ii) a bifunctional molecule, the bifunctional molecule comprising a binding region of non-antibody origin which binds to the antibody of the first species or to one or more non-naturally occurring groups provided thereon, and a constant region from an antibody of a second species, the constant region comprising at least one C<sub>H</sub> domain or an epitope thereof, wherein the bifunctional molecule is bound to a location on the antibody of

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the first species or to one or more non-naturally occurring groups provided thereon, which does not hinder binding between the antibody and its specific antigen.

92. (New) The complex of claim 65, wherein the bifunctional molecule binds to the constant region of the antibody of the first species.

93. (New) The complex of claim 66, wherein the bifunctional molecule binds to the constant region of the antibody of the first species.

94. (New) The complex of claim 73, wherein the bifunctional molecule binds to the constant region of the antibody of the first species.

95. (New) The complex of claim 75, wherein the bifunctional molecule binds to the constant region of the antibody of the first species.

96. (New) The complex of claim 77, wherein the bifunctional molecule binds to the constant region of the antibody of the first species.

97. (New) The complex of claim 79, wherein the bifunctional molecule binds to the constant region of the antibody of the first species.

98. (New) The complex of claim 80, wherein the bifunctional molecule binds to the constant region of the antibody of the first species.

99. (New) The complex of claim 83, wherein the bifunctional molecule binds to the constant region of the antibody of the first species.

100. (New) The complex of claim 90, wherein the bifunctional molecule binds to the constant region of the antibody of the first species.

101. (New) The complex of claim 91, wherein the bifunctional molecule binds to the constant region of the antibody of the first species.

102. (New) A complex formed between (i) an antibody or biologically active fragment thereof from a first species and (ii) a bifunctional molecule, the bifunctional molecule comprising a binding region of non-antibody origin which binds to the antibody of the first species or to one or more non-naturally occurring groups provided thereon, and a constant region from an antibody of a second species, the constant region comprising at least one C<sub>H</sub> domain or an epitope thereof, wherein the bifunctional molecule is bound to the constant region of the antibody of the first species or to one or more non-naturally occurring groups provided thereon.

103. (New) A complex formed between (i) an antibody or biologically active fragment thereof from a first species and (ii) a bifunctional molecule, the bifunctional molecule

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comprising a binding region of non-antibody origin which binds to the antibody of the first species or to one or more non-naturally occurring groups provided thereon, and a constant region from an antibody of a second species, the constant region comprising at least one C<sub>H</sub> domain or an epitope thereof, wherein the bifunctional molecule is bound to the constant region of the antibody of the first species or to one or more non-naturally occurring groups provided thereon, wherein the non-naturally occurring group is a biotin molecule and the binding region comprises streptavidin or a fragment thereof.

104. (New) A complex formed between (i) an antibody or biologically active fragment thereof from a first species and (ii) a bifunctional molecule, the bifunctional molecule comprising a binding region of non-antibody origin which binds to the antibody of the first species or to one or more non-naturally occurring groups provided thereon, and a constant region from an antibody of a second species, the constant region comprising at least one C<sub>H</sub> domain or an epitope thereof, wherein the binding region and the constant region are linked directly or are separated by a linker molecule of between 1 and 20 amino acids in length, and wherein the bifunctional molecule is bound to the constant region of the antibody of the first species or to one or more non-naturally occurring groups provided thereon, wherein the non-naturally occurring group is a biotin molecule and the binding region comprises streptavidin or a fragment thereof.

105. (New) A complex formed between (i) an antibody or biologically active fragment thereof from a first species and (ii) a bifunctional molecule, the bifunctional molecule comprising a binding region of non-antibody origin which binds to the antibody of the first species, and a constant region from an antibody of a second species, the constant region comprising at least one C<sub>H</sub> domain or an epitope thereof, wherein the bifunctional molecule is bound to the constant region of the antibody of the first species.